REMARKS

The present invention is directed to an aqueous ready to use semen extender composition. The semen extender composition includes about 0.1 wt.% to about 6 wt.% phospholipid obtained from non-animal source, about 0.0001 wt.% to about 1 wt.% of anionic surfactant to reduce ice crystal formation during freezing of the composition, about 0.5 wt.% to about 3 wt.% carbohydrate, about 3 wt.% to about 14 wt.% freeze agent, and biological buffer to provide the composition with a pH of about 6.9 to about 7.5, and a sufficient amount of water so that the composition exhibits an osmolality of about 250 mOsM to about 350 mOsM. The claimed invention is additionally directed to a method for manufacturing an aqueous ready to use semen extender composition.

One advantage of the aqueous ready to use semen extender composition according to the present invention is the ability to avoid the use of egg yolk which is a common component in conventional semen extender compositions while providing a semen extender composition that provides a desired level of viability and motility of the sperm cells. It is believed that egg yolk may contain nonpathogenic organisms or pathogenic organisms that may be harmful to the host or cells that contact the product. Accordingly, eliminating egg yolk from the ready to use semen extender composition reduces the risk of contamination of the semen by organisms that may be present in the egg yolk.

The specification of the above-identified patent application includes data demonstrating that the present invention preserves semen comparable to a composition that utilizes egg yolk. The Examiner's attention is directed to example 2 of the above-identified patent application. In particular, tables 8 and 9 on page 19 of the above-identified patent application demonstrate that compositions formulated as aqueous ready to use semen extender compositions containing buffer, carbohydrate, phospholipid (lecithin), and anionic surfactant (Tween 80) perform comparable to a semen extender composition containing egg yolk. Accordingly, the Applicants have developed a semen extender composition that can be used in place of semen extender compositions containing egg yolk.

Rejection Over European Publication No. 0 685 556 (*Ghazarian et al.*)

Claims 1, 2, 6, 8, 11, 13, 14, 21, and 22 stand rejected under 35 U.S.C. §102(b) over *Ghazarian et al.* This rejection is traversed.

Ghazarian et al. fail to disclose an aqueous ready to use semen extender composition containing about 0.0001 wt.% to about 1 wt.% of an anionic surfactant to reduce ice crystal formation during the freezing of the composition according to the present invention. The outstanding Office Action at pages 3-4 contends that "TRIS is also an emulsifying agent as taught by MERCK." The Applicants do not agree with this contention in the outstanding Office Action. TRIS is clearly a buffer and it is used by *Ghazarian et al.* as a buffer and it is taught by the above-identified specification at page 8, lines 1-2, as a buffer. Nevertheless, in order to more clearly distinguish the invention, independent claims 1 and 21 have been amended to characterize the surfactant component as an anionic surfactant.

Because *Ghazarian et al.* fail to disclose an aqueous ready to use semen extender composition containing about 0.0001 wt.% to about 1 wt.% of anionic surfactant to reduce ice crystal formation during freezing of the composition according to the present invention, the claimed invention is not anticipated by *Ghazarian et al.* and withdrawal of this rejection is requested.

Rejection Over U.S. Patent No. 6,368,786 (*Saint-Ramon et al.*)

Claims 1, 2, 4-6, 8, 11, 13, 14, 21, and 22 stand rejected under 35 U.S.C. §102(e) over *Saint-Ramon et al.* This rejection is traversed.

Along with the amendment mailed on March 29, 2005, a Declaration by Dr. Richard Lomneth was provided to demonstrate a reduction to practice of the invention prior to May 14, 1999 corresponding to the priority date of *Saint-Ramon et al.* According to the outstanding Office Action at page 6, the Declaration was dismissed or disregarded on the grounds that "the scope of the showing is different from the scope of instant claims." According to the outstanding Office Action, the claimed invention is drawn to the use of non-animal derived phospholipids whereas "the BILADYL product contains animal derived phospholipids from egg yolk as demonstrated by Exhibit B." See the outstanding Office Action at page 6, lines 8-10. This understanding expressed in the outstanding Office Action is incorrect.

BILADYL is a commercially available product that is intended to be used with egg yolk. The Examiner's attention is directed at Exhibit B provided as part of the Declaration by Dr. Richard Lomneth. A copy of Exhibit B is enclosed. Exhibit B includes instructions for preparing a "cocktail AB." In particular, according to the instructions, "100 ml clean egg yolk

from fresh chicken eggs" is added during the preparation of solution A and during the preparation of solution B. The BILADYL product itself does not contain egg yolk. The BILADYL concentrate referred to in the Declaration by Dr. Richard Lomneth does not contain egg yolk. Accordingly, the interpretation expressed in the outstanding Office Action on page 6 that "the sample 2 composition contains animal derived phospholipids unlike the composition of the instant claims 1 and 21, drawn to the use of non-animal derived phospholipids" is an incorrect statement. Egg yolk was not added to the sample 2 composition reported in the Declaration by Dr. Richard Lomneth. Sample 2 reported in the Declaration by Dr. Richard Lomneth includes lecithin in place of egg yolk.

The Examiner is requested to reconsider the Declaration by Dr. Richard Lomneth in view of the incorrect interpretation of the Declaration expressed in the outstanding Office Action.

The Declaration by Dr. Richard Lomneth clearly demonstrates possession of the invention of the above-identified patent application as a result of a reduction to practice of the invention prior to May 14, 1999. In view of the Declaration by Dr. Richard Lomneth, *Saint-Ramon et al.* does not qualify as prior art under 35 U.S.C. §102(e), and withdrawal of the rejection over *Saint-Ramon et al.* is requested.

Rejection over *Ghazarian et al.* or *Saint-Ramon et al.* in view of U.S. Patent No. 3,444,039 (*Rajamannan*), U.S. Patent No. 6,130,034 (*Aitken*), U.S. Patent No. 6,140,121 (*Ellington et al.*), C. Helleman and E. Gieroux, Deep Freezing of Rabbit Sperm, Effect of a Surfactant on Fertilizing Capacity, Zuchthyg., 23, 33-37 (1988) (*Hellemann et al.*)

Claims 1, 2, 4-6, 8-11, 13, 14, 21, 22, 24-26, and 28-31 stand rejected under 35 U.S.C. §103(a) over *Ghazarian et al.* or *Saint-Ramon et al.* and *Rajamannan*, *Aitken*, *Ellington et al.*, and *Helleman et al.* This rejection is traversed.

In view of the above comments, *Saint-Ramon et al.* are not available as prior art. Accordingly, withdrawal of this rejection as it is based upon *Saint-Ramon et al.* is requested.

As discussed previously, *Ghazarian et al.* fail to disclose an aqueous ready to use semen extender composition comprising about 0.0001 wt.% to about 1 wt.% of anionic surfactant to reduce ice crystal formation during freezing of the composition according to the present invention. It is submitted that the references relied upon in the outstanding Office Action would not have suggested modifying *Ghazarian et al.* to include an anionic surfactant.

Ghazarian et al. are directed to a vehicle for nonautonomous microorganisms of the animal kingdom to be kept alive outside their natural environment with a view to human interventions. The vehicle includes an aqueous medium comprising nutrition agents, buffers and mineral salts, and a protective product formed as a support for embryonic growth by a living organism, wherein the protective product is a lecithin extracted from soy seeds and introduced into the aqueous medium upon formation of the vehicle. See the English language translation of *Ghazarian et al.* on page 2, lines 1-17, and page 3, lines 20-27.

As discussed above, *Ghazarian et al.* fail to disclose a composition containing about 0.0001 wt.% to about 1 wt.% of anionic surfactant to reduce ice crystal formation during freezing of the composition. The outstanding Office Action contends that the TRIS component disclosed by *Ghazarian et al.* satisfies the surfactant component of the claimed composition. TRIS is clearly a buffer and is used as a buffer by *Ghazarian et al.* (see example 1 of *Ghazarian et al.*) and can be used as a buffer according to the present invention (see the above-identified patent application at page 7, lines 1-8). Nevertheless, the independent claims are amended to characterize the surfactant component of the present invention as an anionic surfactant. TRIS is clearly not an anionic surfactant as required by the presently claimed invention.

Rajamannan, *Aitken*, *Ellington et al.*, and *Hellemann et al.* would not have suggested modifying *Ghazarian et al.* to include about 0.0001 wt.% to about 1 wt.% of anionic surfactant to reduce ice crystal formation during freezing of the composition according to the presently claimed invention.

Rajamannan appears to be relied upon in the outstanding Office Action for the disclosure of buffering to a pH of 6 to 7.5 and for the disclosure of sodium citrate as a buffering agent. See *Rajamannan* at column 3, line 30 and lines 41-47. It is pointed out that *Rajamannan* is directed at an egg yolk containing composition. See *Rajamannan* at column 1, lines 13-19, and the example disclosing the presence of egg yolk solids. It is pointed out that *Rajamannan* fails to disclose or suggest the use of about 0.0001 wt.% to about 1 wt.% anionic surfactant to reduce ice crystal formation during freezing of the composition according to the present invention.

It appears that the outstanding Office Action relies upon *Aitken* for the disclosure of an anti-oxidant. *Aitken* refers to an anti-oxidant such as vitamin E at column 1, line 50. It is pointed out, however, that Aitken is directed at an egg yolk-containing system. See *Aitken* at column 1, lines 28-38. The outstanding Office Action fails to explain why one having ordinary

skill in the art would look to a disclosure relating to the use of raw egg yolk for a suggestion to modify a composition that is free of raw egg yolk.

It is submitted that raw egg yolk contains a large number of various components and is a much more complicated system than the semen extender composition that does not contain raw egg yolk. Accordingly, the disclosure of the use of an anti-oxidant in a raw egg containing semen extender composition according to *Aitken* in no way suggests the use of an anti-oxidant in a non-raw egg containing semen extender composition.

Nevertheless, the outstanding Office Action fails to explain why one having ordinary skill in the art would receive a suggestion from *Aitken* to modify *Ghazarian et al.* to include about 0.0001 wt.% to about 1 wt.% anionic surfactant to reduce ice crystal formation during freezing of the composition according to the present invention.

The outstanding Office Action appears to rely on *Ellington et al.* for the disclosure of various buffers such as EDTA and TRIS. See *Ellington et al.* at column 16, lines 52-63, and column 19, line 28. The outstanding Office Action additionally refers to *Ellington et al.* for the disclosure of a balanced culture medium such as M199 at column 16, line 59, and contends that medium M199 suggests the use of polyoxyethylene sorbitan (Tween 80). It is submitted that Tween 80 is provided in medium M199 to help dissolve the other components in medium M199. There is no disclosure by *Ellington et al.* or ATCC Catalogue (Page 522) that Tween 80 can be useful for reducing ice crystal formation during freezing of a semen extender composition. One having ordinary skill in the art would not have received any suggestion from *Ellington et al.* or ATCC Catalogue (Page 522) that the incorporation of Tween 80 into the composition described by *Ghazarian et al.* would have any benefit for reducing ice crystal formation during freezing according to the present invention. Accordingly, no reason has been provided to explain why one having ordinary skill in the art would be motivated to modify *Ghazarian et al.* to include Tween 80 which is simply a disclosed component of medium M199.

The reliance upon *Ellington et al.* and ATCC Catalogue (Page 522) is an example of the use of impermissible hindsight. There must be a suggestion to combine the references or make the modifications to achieve a *prima facie* case of obviousness. It is not enough to simply pick and choose various components from several references. The outstanding Office Action fails to explain why one having ordinary skill in the art would be motivated to select Tween 80 from the lengthy list of components identified in balanced culture M199, and then add that component to

the composition described by *Ghazarian et al.* Clearly, there is no recognition by *Ellington et al.* that an anionic surfactant can be used to reduce ice crystal formation during freezing according to the present invention. Absent a motivation to modify *Ghazarian et al.*, the presently claimed invention would not have been obvious.

Hellemann et al. are apparently relied upon in the outstanding Office Action for the disclosure of sodium laurel sulfate in a composition intended for rabbit semen. See the abstract of *Hellemann et al.* Similar to *Aitken*, *Hellemann et al.* are directed at the use of a composition containing raw egg. It is submitted that one having ordinary skill in the art would not have looked to *Hellemann et al.* for modifying a composition that does not contain raw egg yolk. Furthermore, the outstanding Office Action fails to provide a sufficient reason to explain why one having ordinary skill in the art would modify *Ghazarian et al.* in view of the disclosure by *Hellemann et al.* to achieve the presently claimed invention.

In view of the comments, the presently claimed invention would not have been obvious from *Ghazarian et al.*, *Saint-Ramon et al.*, *Rajamannan*, *Aitken*, *Ellington et al.*, and *Hellemann et al.* Accordingly, withdrawal of this rejection is requested.

It is believed that this application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300

Date: November 1, 2005

Dennis R. Daley
Reg. No. 34,994
DRD:jjb

BILADYL®

Preparation of COCKTAIL AB:

Add 12 ml of double distilled, sterile water, using a sterile syringe.

Final composition of reconstituted COCKTAIL AB expressed as active units of antibiotics per 0.02 ml:
100 µg Tylosin,
500 µg Gentamicin,
300 µg Lincomycin,
600 µg Spectinomycin

Usage for „Neat Semen Treatment":
Add and carefully mix 0,02 ml to each ml of neat semen, using a sterile syringe.

Usage for BILADYL SOLUTION A:
Add and carefully mix 10 ml to SOLUTION A, using a sterile syringe.

Preparation of SOLUTION A:

1) Reconstitute 49 g of SOLUTION A with double distilled sterile water to a combined volume of 390 ml.
2) Add 100 ml clean yolk from fresh chicken eggs.
3) Add 10 ml of reconstituted antibiotics COCKTAIL AB, using a sterile syringe.
4) Mix gently and warm mixture to + 30° C (+ 86° F)
5) Filter medium before adding it to semen.

Preparation of SOLUTION B:

1) Reconstitute 250 g of SOLUTION B with double distilled sterile water to a combined volume of 400 ml.
2) Add 100 ml clean yolk from fresh chicken eggs.
3) Mix gently and warm mixture to + 30° C (+ 86° F)
4) Filter medium before adding it to semen.

Usage:
Dilute semen with equal quantities of SOLUTION A and B according to the CSS Processing Regulations.

Final composition of SOLUTION A and B per 100 ml, as approved by CSS:
Yolk 20 %, Glycerol 7 %, Tris 2,42 %, Citric Acid 1,38 g%, Fructose 1,00 g%, Active Units of Antibiotics:
Tylosin 5,25 mg, Gentamicin 26,25 mg, Lincomycin 15,75 mg, Spectinomycin 31,5 mg and double distilled sterile water

Storage:
At a controlled temperature of + 5° C (+ 41° F) in a dark environment.
Shelf life: 12 months.

Warning:
Keep out of reach of children
Not for human or animal consumption and/or treatment
Not for injection
Not for use on live animals
Do not expose to heat or sun

Made in Germany

BILADYL IS APPROVED BY CERTIFIED SEMEN SERVICES INC.

minitüb

MINITÜB GmbH · Germany
Hauptstraße 41 · 8311 Tiefenbach
Telefon 0 87 09 / 20 77 · Fax 31 90